

SUBSTITUTE SEQUENCE LISTING

<110> Falco, Saverio Carl
 Famodu, Layo
 Rafalski, Jan A.
 Ramaker, Michael
 Tarczynski, Mitchell C.
 Thorpe, Catherine

<120> PLANT METHIONINE SYNTHASE GENE AND METHODS FOR INCREASING THE METHIONINE CONTENT OF THE SEEDS OF PLANTS

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Met Ser Glu Ala Gly Ile Lys Tyr Ile Pro Ser Asn Thr Ser Ser Tyr

Tyr Asp Gln Val Leu Asp Thr Thr Ala Met Leu Gly Ala Val Pro Glu

Arg Tyr Ser Trp Thr Gly Gly Glu Ile Gly Leu Ser Thr Tyr Phe Ser

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Phe Asp Thr Asn Tyr His Phe Ile Val Pro Glu Leu Gly Pro Ser Thr 125

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- Met Ala Arg Gly Asn Ala Thr Val Pro Ala Met Glu Met Thr Lys Trp
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- Glu Thr Tyr Phe Ala Asp Ile Pro Ala Glu Ala Tyr Lys Thr Leu Thr 245 250 255
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Arg Tyr Asn Trp Ala Gly Gly Glu Ile Ala Phe Asp Thr Tyr Phe Ser 85 90 95

Met Ala Arg Gly Asn Ala Ser Val Pro Ala Met Glu Met Thr Lys Trp
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Phe Asp Thr Asn Tyr His Phe Ile Val Pro Glu Leu Gly Pro Asp Val

Asn Phe Ser Tyr Ala Ser His Lys Ala Val Asp Glu Tyr Lys Glu Ala 130 135 140

Lys Gly Leu Gly Val Asp Thr Val Pro Val Leu Ile Gly Pro Val Ser 145 150 155 160

Tyr Leu Leu Ser Lys Pro Ala Lys Gly Val Glu Lys Ser Phe Pro 165 170 175

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Thr Leu Val Leu Asp Leu Gln Ala His Gln Leu Glu Ala Phe Thr Lys 210 215 220

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Tyr Asp Gln Val Leu Asp Thr Thr Ala Met Leu Gly Ala Val Pro Asp
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Asp Ala Gln Gln Lys Lys Leu Asn Leu Pro Ile Leu Pro Thr Thr
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Ile Gly Ser Phe Pro Gln Thr Met Asp Leu Arg Arg Val Arg Arg Glu

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Tyr Lys Ala Lys Glu Asp Leu Xaa Xaa Gly Val Cys Gln Cys Tyr Gln 65 70 75 80

Gly Arg Asn Xaa Gln Arg Leu Ser Arg Phe Lys Glu Glu Leu Asp Ile 85 90 95

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Tyr Asp Gln Val Leu Asp Thr Ala Thr Met Leu Gly Ala Val Pro Pro 65 70 75 80

Arg Tyr Asn Phe Ala Gly Glu Ile Gly Phe Asp Thr Tyr Phe Ser 85 90 95

Met Ala Arg Gly Asn Ala Ser Val Pro Ala Met Glu Met Thr Lys Trp
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Phe Asp Thr Asn Tyr His Tyr Ile Val Pro Glu Leu Gly Pro Glu Val

Asn Phe Ser Tyr Ala Ser His Lys Ala Val Asn Glu Tyr Lys Glu Ala 130 135 140

Lys Glu Leu Gly Val Asp Thr Val Pro Val Leu Val Gly Pro Val Thr 145 150 155 160

Phe Leu Leu Ser Lys Pro Ala Lys Gly Val Glu Lys Thr Phe Pro 165 170 175

Leu Leu Ser Leu Leu Asp Lys Ile Leu Pro Val Tyr Lys Glu Val Ile 180 185 190

Gly Glu Leu Lys Ala Ala Gly Ala Ser Trp Ile Gln Phe Asp Glu Pro 195 200 205

Thr Leu Val Leu Asp Leu Glu Ser His Gln Leu Glu Ala Phe Thr Lys 210 220

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540

535

530

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Pro Leu Pro Pro Ser Ser Ala Ser Arg Gln Thr Ser Ser Ala Ser Ala 50 55 60

Ala Ala Asp Val Ser Ala Ile Pro Asn Ala Lys Val Ala Gln Pro Ser 65 70 75 80

Ala Val Val Leu Ala Glu Arg Asn Leu Leu Gly Ser Asp Ala Ser Leu 85 90 95

Ala Val His Ala Gly Glu Arg Leu Gly Arg Arg Ile Ala Thr Asp Ala 100 105 110

Ile Thr Thr Pro Val Val Asn Thr Ser Ala Tyr Trp Phe Asn Asn Ser 115 120 125

Gln Glu Leu Ile Asp Phe Lys Glu Gly Arg His Ala Ser Phe Glu Tyr 130 135 140

Gly Arg Tyr Gly Asn Pro Thr Thr Glu Ala Leu Glu Lys Lys Met Ser

Ala Leu Glu Lys Ala Glu Ser Thr Val Phe Val Ala Ser Gly Met Tyr 165 170 175

Ala Ala Val Ala Met Leu Ser Ala Leu Val Pro Ala Gly Gly His Ile 180 185 190

Val Thr Thr Asp Cys Tyr Arg Lys Thr Arg Ile Tyr Met Glu Asn 195 200 205

Glu Leu Pro Lys Arg Gly Ile Ser Met Thr Val Ile Arg Pro Ala Asp 210 215 220

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Met Ala Thr Val Ser Leu Thr Pro Gln Ala Val Phe Ser Thr Glu Ser

Gly Gly Ala Leu Ala Ser Ala Thr Ile Leu Arg Phe Pro Pro Asn Phe

25

20

- Val Arg Gln Leu Ser Thr Lys Ala Arg Arg Asn Cys Ser Asn Ile Gly 35 40 45
- Val Ala Gln Ile Val Ala Ala Ala Trp Ser Asp Cys Pro Ala Ala Arg
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- Pro His Leu Gly Gly Gly Arg Arg Ala Arg Gly Val Ala Ser Ser 65 70 75 80
- His Ala Ala Ala Ala Ser Ala Ala Ala Ala Ala Ser Ala Ala Glu 85 90 95
- Val Ser Ala Ile Pro Asn Ala Lys Val Ala Gln Pro Ser Ala Val Val 100 105 110
- Leu Ala Glu Arg Asn Leu Leu Gly Ser Asp Ala Ser Leu Ala Val His
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- Ala Gly Glu Arg Leu Gly Arg Arg Ile Ala Thr Asp Ala Ile Thr Thr 130 135 140
- Pro Val Val Asn Thr Ser Ala Tyr Trp Phe Asn Asn Ser Gln Glu Leu 145 150 155 160
- Ile Asp Phe Lys Glu Gly Arg His Ala Ser Phe Glu Tyr Gly Arg Tyr
 165 170 175
- Gly Asn Pro Thr Thr Glu Ala Leu Glu Lys Lys Met Ser Ala Leu Glu 180 185 190
- Lys Ala Glu Ser Thr Val Phe Val Ala Ser Gly Met Tyr Ala Ala Val 195 200 205
- Ala Met Leu Ser Ala Leu Val Pro Ala Gly Gly His Ile Val Thr Thr 210 215 220
- Thr Asp Cys Tyr Arg Lys Thr Arg Ile Tyr Met Glu Asn Glu Leu Pro
- Lys Arg Gly Ile Ser Met Thr Val Ile Arg Pro Ala Asp Met Asp Ala 245 250 255
- Leu Gln Asn Ala Leu Asp Asn Asn Asn Val Ser Leu Phe Phe Thr Glu 260 265 270
- Thr Pro Thr Asn Pro Phe Leu Arg Cys Ile Asp Ile Glu His Val Ser 275 280 285
- Asn Met Cys His Ser Lys Gly Ala Leu Leu Cys Ile Asp Ser Thr Phe 290 295 300
- Ala Ser Pro Ile Asn Gln Lys Ala Leu Thr Leu Gly Ala Asp Leu Val 305 310 315 320
- Ile His Ser Ala Thr Lys Tyr Ile Ala Gly His Asn Asp Val Ile Gly 325 330 335
- Gly Cys Val Ser Gly Arg Asp Glu Leu Val Ser Lys Val Arg Ile Tyr 340 345 350

His His Val Val Gly Gly Val Leu Asn Pro Asn Ala Ala Tyr Leu Ile Leu Arg Gly Met Lys Thr Leu His Leu Arg Val Gln Cys Gln Asn Asp 375 380 370 Thr Ala Leu Arg Met Ala Gln Phe Leu Glu Glu His Pro Lys Ile Ala 390 395 Arg Val Tyr Tyr Pro Gly Leu Pro Ser His Pro Glu His His Ile Ala Lys Ser Gln Met Thr Gly Phe Gly Gly Val Val Ser Phe Glu Val Ala Gly Asp Phe Asp Ala Thr Arg Lys Phe Ile Asp Ser Val Lys Ile Pro Tyr His Ala Pro Ser Phe Gly Gly Cys Glu Ser Ile Ile Asp Gln Pro Ala Ile Met Ser Tyr Trp Asp Ser Lys Glu Gln Arg Asp Ile Tyr Gly 470 475 Ile Lys Asp Asn Leu Ile Arg Phe Ser Ile Gly Val Glu Asp Phe Glu Asp Leu Lys Asn Asp Leu Val Gln Ala Leu Glu Lys Ile 505 <210> 20 <211> 14 <212> DNA <213> Artificial Sequence <223> Description of Artificial Sequence: Synthetic oligonucleotide <400> 20 aattcatgag tgca 14 <210> 21 <211> 14 <212> DNA <213> Artificial Sequence <223> Description of Artificial Sequence: Synthetic oligonucleotide <400> 21 aatttgcact catg 14 <210> 22 <211> 1350 <212> DNA <213> Escherichia coli <400> 22 atggctgaaa ttgttgtctc caaatttggc ggtaccagcg tagctgattt tgacgccatg aaccgcagcg ctgatattgt gctttctgat gccaacgtgc gtttagttgt cctctcggct 120

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Val Ala Leu Ala Glu Gly Leu Glu Pro Gly Glu Arg Phe Glu Lys Leu 50 55 60

Asp Ala Ile Arg Asn Ile Gln Phe Ala Ile Leu Glu Arg Leu Arg Tyr 65 70 75 80

Pro Asn Val Ile Arg Glu Glu Ile Glu Arg Leu Leu Glu Asn Ile Thr 85 90 95

Val Leu Ala Glu Ala Ala Ala Leu Ala Thr Ser Pro Ala Leu Thr Asp 100 105 110

Glu Leu Val Ser His Gly Glu Leu Met Ser Thr Leu Leu Phe Val Glu 115 120 125

Ile Leu Arg Glu Arg Asp Val Gln Ala Gln Trp Phe Asp Val Arg Lys 130 135 140

Val Met Arg Thr Asn Asp Arg Phe Gly Arg Ala Glu Pro Asp Ile Ala 145 150 155 160

Ala Leu Ala Glu Leu Ala Ala Leu Gln Leu Pro Arg Leu Asn Glu
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Gly Leu Val Ile Thr Gln Gly Phe Ile Gly Ser Glu Asn Lys Gly Arg 180 185 190

Thr Thr Leu Gly Arg Gly Gly Ser Asp Tyr Thr Ala Ala Leu Leu 195 200 205

Ala Glu Ala Leu His Ala Ser Arg Val Asp Ile Trp Thr Asp Val Pro 210 215 220

Gly Ile Tyr Thr Thr Asp Pro Arg Val Val Ser Ala Ala Lys Arg Ile 225 230 235 240

Asp Glu Ile Ala Phe Ala Glu Ala Ala Glu Met Ala Thr Phe Gly Ala 245 250 255

Lys Val Leu His Pro Ala Thr Leu Leu Pro Ala Val Arg Ser Asp Ile 260 265 270

Pro Val Phe Val Gly Ser Ser Lys Asp Pro Arg Ala Gly Gly Thr Leu 275 280 285

Val Cys Asn Lys Thr Glu Asn Pro Pro Leu Phe Arg Ala Leu Ala Leu 290 295 300

Arg Arg Asn Gln Thr Leu Leu Thr Leu His Ser Leu Asn Met Leu His 305 310 315 320

Ser Arg Gly Phe Leu Ala Glu Val Phe Gly Ile Leu Ala Arg His Asn 325 330 335

Ile Ser Val Asp Leu Ile Thr Thr Ser Glu Val Ser Val Ala Leu Thr 340 345 350

Leu Asp Thr Thr Gly Ser Thr Ser Thr Gly Asp Thr Leu Leu Thr Gln 355

Ser Leu Leu Met Glu Leu Ser Ala Leu Cys Arg Val Glu Val Glu Glu 370 375 380

Gly Leu Ala Leu Val Ala Leu Ile Gly Asn Asp Leu Ser Lys Ala Cys 385 390 395 400

Ala Val Gly Lys Glu Val Phe Gly Val Leu Glu Pro Phe Asn Ile Arg
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Met Ile Cys Tyr Gly Ala Ser Ser His Asn Leu Cys Phe Leu Val Pro 420 425 430

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<212> PRT

<213> Zea mays

<400> 29

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Met Pro Leu Ala Thr Met Asn Pro Trp Met Gln Tyr Cys Met Lys Gln 35 40 45

Gln Gly Val Ala Asn Leu Leu Ala Trp Pro Thr Leu Met Leu Gln Gln 50 55 60

Leu Leu Ala Ser Pro Leu Gln Gln Cys Gln Met Pro Met Met Pro 65 70 75 80

Gly Met Met Pro Pro Met Thr Met Met Pro Met Pro Ser Met Met Pro 85 90 95

Ser Met Met Val Pro Thr Met Met Ser Pro Met Thr Met Ala Ser Met 100 105 . 110

Met Pro Pro Met Met Met Pro Ser Met Ile Ser Pro Met Thr Met Pro 115 120 125

Ser Met Met Pro Ser Met Ile Met Pro Thr Met Met Ser Pro Met Ile 130 135 140

Met Pro Ser Met Met Pro Pro Met Met Met Pro Ser Met Val Ser Pro 145 150 155 160

Met Met Met Pro Asn Met Met Thr Val Pro Gln Cys Tyr Ser Gly Ser 165 170 175

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Ile Ser His Ile Ile Gln Gln Gln Leu Pro Phe Met Phe Ser Pro
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                                185
                                                     190
Thr Ala Met Ala Ile Pro Pro Met Phe Leu Gln Gln Pro Phe Val Gly
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                                                 205
Ala Ala Phe
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tgatgctgca gcaactgttg gcctcaccgc ttcagcagtg ccagatgcca atgatgatgc 240
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<213> Zea mays
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                                      10
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caatgatgat gccaaacatg atgacagtgc cacaatgtta ctctggttct atctcacaca 480
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Asn Leu Leu Ala Trp Pro Thr Leu Met Leu Gln Gln Leu Leu Ala Ser
         35
                             40
                                                 45
Pro Leu Gln Gln Cys Gln Met Pro Met Met Pro Gly Met Met Pro
                         55
Pro Met Thr Met Met Pro Met Pro Ser Met Met Pro Ser Met Wal
65
                     70
                                         75
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Pro Thr Met Met Ser Pro Met Thr Met Ala Ser Met Met Pro Pro Met
                 85
                                     90
Met Met Pro Ser Met Ile Ser Pro Met Thr Met Pro Ser Met Met Pro
                                105
Ser Met Ile Met Pro Thr Met Met Ser Pro Met Ile Met Pro Ser Met
        115
                            120
                                                125
Met Pro Pro Met Met Pro Ser Met Val Ser Pro Met Met Pro
Asn Met Met Thr Val Pro Gln Cys Tyr Ser Gly Ser Ile Ser His Ile
                    150
                                        155
Ile Gln Gln Gln Leu Pro Phe Met Phe Ser Pro Thr Ala Met Ala
Ile Pro Pro Met Phe Leu Gln Gln Pro Phe Val Gly Ala Ala Phe
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                                                                  43
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<211> 55
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<211> 55
<212> DNA
<213> Artificial Sequence
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<210> 45
<211> 59
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<210> 46
<211> 75
<212> DNA
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<210> 47
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<211> 90
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catggttgct ccattcaccg gcctcaaaag
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<210> 49
<211> 90
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<210> 50
<211> 31
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<213> Glycine max
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<221> unsure
<222> (1461)
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<220>
<221> unsure
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cctcaacccc tctcccctta tttttcccaa ctcctgtttt ccctaatgaa tgttgtatct 1440
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- Arg Glu Glu Leu Leu Ala Val Gly Arg Glu Leu Arg Ala Arg His Trp 35 40 45
- Asp Gln Gln Lys Gln Ala Gly Ile Asp Leu Pro Val Gly Asp Phe 50 55 60
- Ala Trp Tyr Asp His Val Leu Thr Thr Ser Leu Leu Gly Asn Val 65 70 75 80
- Pro Ala Arg His Gln Asn Lys Asp Gly Ser Val Asp Ile Asp Thr Leu 85 90 95
- Phe Arg Ile Gly Arg Gly Arg Ala Pro Thr Gly Glu Pro Ala Ala Ala 100 105 110
- Ala Glu Met Thr Lys Trp Phe Asn Thr Asn Tyr His Tyr Met Val Pro 115 120 125
- Glu Phe Val Lys Gly Gln Gln Phe Lys Leu Thr Trp Thr Gln Leu Leu 130 135 140
- Asp Glu Val Asp Glu Ala Leu Ala Leu Gly His Lys Val Lys Pro Val 145 150 155 160
- Leu Leu Gly Pro Val Thr Trp Leu Trp Leu Gly Lys Val Lys Gly Glu
 165 170 175
- Gln Phe Asp Arg Leu Ser Leu Leu Asn Asp Ile Leu Pro Val Tyr Gln 180 185 190
- Gln Val Leu Ala Glu Leu Ala Lys Arg Gly Ile Glu Trp Val Gln Ile 195 200 205
- Asp Glu Pro Ala Leu Val Leu Glu Leu Pro Gln Ala Trp Leu Asp Ala 210 215 220
- Tyr Lys Pro Ala Tyr Asp Ala Leu Gln Gly Gln Val Lys Leu Leu 225 230 235 240
- Thr Thr Tyr Phe Glu Gly Val Thr Pro Asn Leu Asp Thr Ile Thr Ala 245 250 255
- Leu Pro Val Gln Gly Leu His Val Asp Leu Val His Gly Lys Asp Asp 260 265 270
- Val Ala Glu Leu His Lys Arg Leu Pro Ser Asp Trp Leu Leu Ser Ala 275 280 285

- Gly Leu Ile Asn Gly Arg Asn Val Trp Arg Ala Asp Leu Thr Glu Lys 290 295 300
- Tyr Ala Gln Ile Lys Asp Ile Val Gly Lys Arg Asp Leu Trp Val Ala 305 310 315 320
- Ser Ser Cys Ser Leu Leu His Ser Pro Ile Asp Leu Ser Val Glu Thr 325 330 335
- Arg Leu Asp Ala Glu Val Lys Ser Trp Phe Ala Phe Ala Leu Gln Lys 340 345 350
- Cys His Glu Leu Ala Leu Leu Arg Asp Ala Leu Asn Ser Gly Asp Thr 355 360 365
- Ala Ala Leu Ala Glu Trp Ser Ala Pro Ile Gln Ala Arg Arg His Ser 370 375 380
- Thr Arg Val His Asn Pro Ala Val Glu Lys Arg Leu Ala Ala Ile Thr 385 390 395 400
- Ala Gln Asp Ser Gln Arg Ala Asn Val Tyr Glu Val Arg Ala Glu Ala 405 410 415
- Gln Arg Ala Arg Phe Lys Leu Pro Ala Trp Pro Thr Thr Ile Gly
 420 425 430
- Ser Phe Pro Gln Thr Thr Glu Ile Arg Thr Leu Arg Leu Asp Phe Lys 435 440 445
- Lys Gly Asn Leu Asp Ala Asn Asn Tyr Arg Thr Gly Ile Ala Glu His 450 455 460
- Ile Lys Gln Ala Ile Val Glu Gln Glu Arg Leu Gly Leu Asp Val Leu 465 470 475 480
- Val His Gly Glu Ala Glu Arg Asn Asp Met Val Glu Tyr Phe Gly Glu
 485 490 495
- His Leu Asp Gly Phe Val Phe Thr Gln Asn Gly Trp Val Gln Ser Tyr 500 505 510
- Gly Ser Arg Cys Val Lys Pro Pro Ile Val Ile Gly Asp Ile Ser Arg 515 520 525
- Pro Ala Pro Ile Thr Val Glu Trp Ala Lys Tyr Ala Gln Ser Leu Thr 530 535 540
- Asp Lys Pro Val Lys Gly Met Leu Thr Gly Pro Val Thr Ile Leu Cys 545 550 550 555
- Trp Ser Phe Pro Arg Glu Asp Val Ser Arg Glu Thr Ile Ala Lys Gln 565 570 575
- Ile Ala Leu Ala Cys Val Met Lys Trp Pro Ile Trp Lys Pro Leu Glu 580 585 590
- Leu Ala Ser Ser Arg Leu Thr Asn Arg Arg Leu Arg Gln Gly Leu Pro 595 600 605

Leu Arg Arg Ser Asp Trp Asp Ala Tyr Leu Gln Trp Gly Val Glu Ala 610 615 620

Phe Arg Ile Asn Ala Ala Val Ala Lys Asp Asp Thr Gln Ile His Thr 625 630 635 640

His Met Cys Tyr Cys Glu Phe Asn Asp Ile Met Asp Ser Ile Ala Ala 645 650 655

Leu Asp Arg Asp Val Ile Thr Ile Glu Thr Ser Arg Ser Asp Met Glu
660 665 670

Leu Leu Glu Ser Phe Glu Glu Phe Asp Tyr Pro Asn Glu Ile Gly Pro 675 680 685

Gly Val Tyr Asp Ile His Ser Pro Asn Val Pro Ser Val Glu Trp Ile 690 695 700

Glu Ala Leu Leu Lys Lys Ala Ala Lys Arg Ile Pro Ala Glu Arg Leu 705 710 715 720

Trp Val Asn Pro Asp Cys Gly Leu Lys Thr Arg Gly Trp Pro Glu Thr 725 730 735

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Gly

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Asp Glu Leu Phe Lys Val Gly Lys Asp Leu Arg Thr Gln Asn Trp Lys 35 40 45

Leu Gln Lys Glu Ala Gly Val Asp Ile Ile Pro Ser Asn Asp Phe Ser 50 55 60

Phe Tyr Asp Gln Val Leu Asp Leu Ser Leu Leu Phe Asn Val Ile Pro 65 70 75 80

Asp Arg Tyr Thr Lys Tyr Asp Leu Ser Pro Ile Asp Thr Leu Phe Ala
85 90 95

Met Gly Arg Gly Leu Gln Arg Lys Ala Thr Glu Thr Glu Lys Ala Val 100 105 110

Asp Val Thr Ala Leu Glu Met Val Lys Trp Phe Asp Ser Asn Tyr His
115 120 125

Tyr Val Arg Pro Thr Phe Ser Lys Thr Thr Gln Phe Lys Leu Asn Gly 130 135 Gln Lys Pro Val Asp Glu Phe Leu Glu Ala Lys Glu Leu Gly Ile His 150 Thr Arg Pro Val Leu Leu Gly Pro Val Ser Tyr Leu Phe Leu Gly Lys 170 Ala Asp Lys Asp Ser Leu Asp Leu Glu Pro Leu Ser Leu Leu Glu Gln 185 Leu Leu Pro Leu Tyr Thr Glu Ile Leu Ser Lys Leu Ala Ser Ala Gly Ala Thr Glu Val Gln Ile Asp Glu Pro Val Leu Val Leu Asp Leu Pro 215 Ala Asn Ala Gln Ala Ala Ile Lys Lys Ala Tyr Thr Tyr Phe Gly Glu Gln Ser Asn Leu Pro Lys Ile Thr Leu Ala Thr Tyr Phe Gly Thr Val Val Pro Asn Leu Asp Ala Ile Lys Gly Leu Pro Val Ala Ala Leu His 265 Val Asp Phe Val Arg Ala Pro Glu Gln Phe Asp Glu Val Val Ala Ala Ile Gly Asn Lys Gln Thr Leu Ser Val Gly Ile Val Asp Gly Arg Asn 295 Ile Trp Lys Asn Asp Phe Lys Lys Ser Ser Ala Ile Val Asn Lys Ala Ile Glu Lys Leu Gly Ala Asp Arg Val Val Val Ala Thr Ser Ser Ser Leu Leu His Thr Pro Val Asp Leu Asn Asn Glu Thr Lys Leu Asp Ala Glu Ile Lys Gly Phe Phe Ser Phe Ala Thr Gln Lys Leu Asp Glu Val Val Val Ile Thr Lys Asn Val Ser Gly Gln Asp Val Ala Ala Leu 375 Glu Ala Asn Ala Lys Ser Val Glu Ser Arg Gly Lys Ser Lys Phe Ile 390 395 His Asp Ala Ala Val Lys Arg Arg Val Ala Ser Ile Asp Glu Lys Met 405 410 Ser Thr Arg Ala Ala Pro Phe Glu Gln Arg Leu Pro Glu Gln Gln Lys 425 Val Phe Asn Leu Pro Leu Phe Pro Thr Thr Ile Gly Ser Phe Pro

445

440

435

- Gln Thr Lys Asp Ile Arg Ile Asn Arg Asn Lys Phe Asn Lys Gly Thr Ile Ser Ala Glu Glu Tyr Glu Lys Phe Ile Asn Ser Glu Ile Glu Lys Val Ile Arg Phe Gln Glu Glu Ile Gly Leu Asp Val Leu Val His Gly Glu Pro Glu Arg Asn Asp Met Val Gln Tyr Phe Gly Glu Gln Ile Asn 505 Gly Tyr Ala Phe Thr Val Asn Gly Trp Val Gln Ser Tyr Gly Ser Arg 520 Tyr Val Arg Pro Pro Ile Ile Val Gly Asp Leu Ser Arg Pro Lys Ala 535 Met Ser Val Lys Glu Ser Val Tyr Ala Gln Ser Ile Thr Ser Lys Pro 555 Val Lys Gly Met Leu Thr Gly Pro Ile Thr Cys Leu Arg Trp Ser Phe 570
- Pro Arg Asp Asp Val Asp Gln Lys Thr Gln Ala Met Gln Leu Ala Leu 585
- Ala Leu Arg Asp Glu Val Asn Asp Leu Glu Ala Ala Gly Ile Lys Val
- Ile Gln Val Asp Glu Pro Ala Leu Arg Glu Gly Leu Pro Leu Arg Glu
- Gly Thr Glu Arg Ser Ala Tyr Tyr Thr Trp Ala Ala Glu Ala Phe Arg 635
- Val Ala Thr Ser Gly Val Ala Asn Lys Thr Gln Ile His Ser His Phe 650 645
- Cys Tyr Ser Asp Leu Asp Pro Asn His Ile Lys Ala Leu Asp Ala Asp 665
- Val Val Ser Ile Glu Phe Ser Lys Lys Asp Asp Ala Asn Tyr Ile Ala 680
- Glu Phe Lys Asn Tyr Pro Asn His Ile Gly Leu Gly Leu Phe Asp Ile 695
- His Ser Pro Arg Ile Pro Ser Lys Asp Glu Phe Ile Ala Lys Ile Ser 710 715
- Thr Ile Leu Lys Ser Tyr Pro Ala Glu Lys Phe Trp Val Asn Pro Asp 725
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- His Met Val Glu Ala Ala Lys Tyr Phe Arg Glu Gln Tyr Lys Asn 755 760 765

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Met Ala Asp Ala Gly Ile Lys Tyr Ile Pro Xaa Asn Thr Phe Ser Tyr
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Tyr 65	Asp	Gln	Val	Leu	Asp 70	Thr	Thr	Ala	Met	Leu 75	Gly	Ala	Val	Pro	Ala 80
Arg	Tyr	Asn	Trp	Ala 85	Gly	Gly	Glu	Ile	Ala 90	Phe	Asp	Thr	Tyr	Phe 95	Ser
Met	Ala	Arg	Gly 100	Asn	Xaa	Ser	Val	Pro 105	Ala	Met	Glu	Met	Thr 110	Lys	Trp
Xaa	Asp	Thr 115	Asn	Tyr	His	Phe	Ile 120	Val	Pro	Glu	Leu	Gly 125	Pro	Asp	Val
Asn	Phe 130	Ser	Tyr	Ala	Ser	His 135	Lys	Ala	Val	Asp	Glu 140	Tyr	Lys	Glu	Ala
Lys 145	Gly	Leu	Gly	Val	Asp 150	Thr	Val	Pro	Val	Leu 155	Ile	Gly	Pro	Val	Ser 160
Tyr	Leu	Leu	Leu	Ser 165	Lys	Pro	Ala	Lys	Gly 170	Val	Glu	Lys	Ser	Phe 175	Pro
Leu	Leu	Ser	Leu 180	Leu	Asp	Lys	Val	Leu 185	Pro	Ile	Tyr	Lys	Glu 190	Val	Ile
Ala	Glu	Leu 195	Lys	Ala	Ala	Gly	Ala 200	Ser	Trp	Ile	Gln	Phe 205	Asp	Glu	Pro
Thr	Leu 210	Val	Leu	Asp	Leu	Gln 215	Ala	His	Gln	Leu	Glu 220	Ala	Phe	Thr	Lys
Ala 225	Tyr	Ala	Glu	Leu	Glu 230	Ser	Ser	Leu	Ser	Gly 235	Leu	Asn	Val	Leu	Thr 240
Glu	Thr	Tyr	Phe	Ala 245	Asp	Val	Pro	Ala	Glu 250	Ala	Phe	Lys	Thr	Leu 255	Thr
Ala	Leu	Lys	Gly 260	Val	Thr	Ala	Phe	Gly 265	Phe	Asp	Leu	Val	Arg 270	Gly	Ala
Gln	Thr	Leu 275	Asp	Leu	Ile	Lys	Gly 280	Gly	Phe	Pro	Ser	Gly 285	Lys	Tyr	Leu
Phe	Ala 290	Gly	Val	Val	Asp	Gly 295	Arg	Asn	Ile	Trp	Ala 300	Asn	Asp	Leu	Ala
Ala 305	Ser	Leu	Asn	Leu	Leu 310	Gln	Ser	Leu	Glu	Gly 315	Ile	Val	Gly	Lys	Asp 320
Lys	Leu	Val	Val	Ser 325	Thr	Ser	Cys	Ser	Leu 330	Leu	His	Thr	Ala	Val 335	Asp
Leu	Val	Asn	Glu 340	Thr	Lys	Leu	Asp	Asp 345	Glu	Ile	Lys	Ser	Trp 350	Leu	Ala
Phe	Ala	Ala 355	Gln	Lys	Val	Val	Glu 360	Val	Asn	Ala	Leu	Ala 365	Lys	Ala	Leu
Ala	Xaa 370	His	Lys	Asp	Glu	Ala 375	Phe	Phe	Ser	Ala	Asn 380	Ala	Thr	Ala	Gln

Ala Ser Arg Lys Ser Ser Pro Arg Val Thr Asn Glu Ala Val Gln Lys 395 Ala Ala Ala Leu Lys Gly Ser Asp His Arg Arg Ala Thr Asn Val 405 410 Ser Ser Arg Leu Asp Ala Gln Gln Lys Lys Leu Asn Leu Pro Val Leu 425 Pro Thr Thr Ile Gly Ser Phe Pro Gln Thr Val Glu Leu Arg Arg 440 Val Arg Arg Glu Tyr Lys Ala Lys Lys Ile Ser Glu Glu Glu Tyr Val Lys Ala Ile Lys Ala Glu Ile Lys Lys Val Val Asp Leu Gln Glu Glu Leu Asp Ile Asp Val Leu Val His Gly Glu Pro Glu Arg Asn Asp Met Val Glu Tyr Phe Gly Glu Gln Leu Ser Gly Phe Ala Phe Thr Ala Asn Gly Trp Val Gln Ser Tyr Gly Ser Arg Cys Val Lys Pro Pro Ile Ile Tyr Gly Asp Val Ser Arg Pro Asn Pro Met Thr Val Phe Trp Ser Lys 535 Thr Ala Gln Ser Met Thr Lys Arg Pro Met Lys Gly Met Leu Thr Gly 555 Pro Val Thr Ile Leu Asn Trp Ser Phe Val Arg Asn Asp Gln Pro Arg Xaa Glu Thr Cys Tyr Gln Ile Ala Xaa Xaa Ile Lys Asp Glu Val Glu Asp Leu Glu Lys Ala Xaa Ile Thr Val Ile Gln Ile Asp Glu Ala Ala Leu Arg Glu Gly Leu Pro Leu Arg Lys Ala Glu His Ala Phe Tyr Leu Asn Trp Ala Val His Ser Phe Arg Ile Thr Asn Val Gly Ile Gln Asp 630 635 Thr Thr Gln Ile His Thr His Met Cys Tyr Ser Asn Phe Asn Asp Ile 645 Ile His Ser Ile Ile Asp Met Asp Ala Asp Val Ile Thr Ile Glu Asn 665 Ser Arg Ser Asp Glu Lys Leu Leu Ser Val Phe Arg Glu Gly Val Lys 675 680 Tyr Gly Ala Gly Ile Gly Pro Gly Val Tyr Asp Ile His Ser Pro Arg 695 700

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Ile Pro Ser Thr Glu Glu Ile Ala Asp Arg Val Asn Lys Met Leu Ala
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Val Leu Asp Thr Asn Ile Leu Trp Val Asn Pro Asp Cys Gly Leu Lys
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Thr Arg Lys Tyr Ala Glu Val Lys Pro Ala Leu Glu Asn Met Val Ser
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Ala Phe Ala Ser Thr Ala Thr Gly Trp Xaa Xaa Ser Tyr Gly Ser Arg
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Ala Ala Ala Leu Lys Gly Ser Asp His Arg Arg Ala Thr Asn Val
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Ser Ala Arg Leu Asp Ala Gln Gln Lys Lys Leu Asn Leu Ser Val Leu Pro Thr Thr Ile Gly Ser Phe Pro Gln Thr Ala Asp Leu Arg Arg Val Arg Arg Glu Phe Lys Ala Asn Lys Ile Ser Glu Glu Glu Tyr Val Lys Ser Ile Lys Glu Glu Ile Arg Lys Val Val Glu Leu Gln Glu Glu Leu Asp Ile Asp Val Leu Val His Gly Glu Pro Glu Arg Asn Asp Met Val Glu Tyr Phe Gly Glu Gln Leu Ser Gly Phe Ala Phe Thr Val Asn Gly Trp Val Gln Ser Tyr Gly Ser Arg Cys Val Lys Pro Pro Ile Ile 170 Tyr Gly Asp Val Ser Arg Pro Lys Pro Met Thr Val Phe Trp Ser Ser 185 Leu Ala Gln Ser Phe Thr Lys Arg Pro Met Lys Gly Met Leu Thr Gly Pro Val Thr Ile Leu Asn Trp Xaa Phe Val Arg Asn Asp Gln Pro Arg Ser Glu Thr Thr Tyr Gln Ile Ala Leu Ala Ile Lys Asp Glu Val Glu Asp Leu Glu Lys Ala Gly Ile Thr Val Ile Gln Ile Asp Glu Ala Ala Leu Arg Glu Gly Leu Pro Leu Xaa Lys Ser Glu Gln Ala His Tyr Leu 265 Asp Trp Ala Val His Ala Phe Arg Ile Thr Asn Val Gly Val Gln Asp 280 Thr Thr Gln Ile His Thr His Met Cys Tyr Ser Asn Phe Asn Asp Ile 295 Ile His Ser Ile Ile Asp Met Asp Ala Asp Val Ile Thr Ile Glu Asn 310 315 Ser Arg Ser Asp Glu Lys Leu Leu Ser Val Phe Arg Glu Gly Val Lys 325 330 335 Tyr Gly Ala Gly Ile Xaa Pro Gly Val Tyr Asp Ile His Ser Pro Arg 345 Ile Pro Pro Thr Glu Glu Ile Ala Asp Arg Ile Asn Lys Met Leu Ala 355 Val Leu Glu Lys Asn Ile Leu Trp Val Asn Pro Asp Cys Gly Leu Lys 380

Thr Arg Lys Tyr Thr Glu Val Lys Pro Ala Leu Thr Asn Met Val Ala 385 390 395 400

Ala Ala Lys Leu Ile Arg Asn Glu Leu Ala Lys 405 410